REMARKS

Claims 32-63 and 92-123 are pending in the present application. Claims 32, 39, 58, 60, 62, 92, 95, 101, and 122 have been amended to correct minor typographical errors and more particularly point out and distinctly claim the invention. No new matter is added by these amendments.

The Rejection Under 35 U.S.C. § 112

Claim 61 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Office Action states that claim 61 recites "the flavoring agent" in the composition of claim 32, but that there is insufficient antecedent basis for this limitation in the claim. Applicant believes that the Office Action meant to refer to claim 60, as claim 61 does not recite "the flavoring agent." Applicant has amended the dependency of claim 60 to overcome any § 112 rejection. Accordingly, the § 112, second paragraph, rejection should be withdrawn.

The Rejection Under 35 U.S.C. § 103(b)

Claims 32, 36-59, 61-63, 92 and 97-123 stand rejected under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,719,197 to Kanios et al. ("Kanios") in view of U.S. Patent No. 5,605,674 ("Purewal et al."). Applicant respectfully traverses.

Applicant submits that the Office Action has not made out a *prima facie* case of obviousness. The Applicant's claims are directed to buccal spray compositions and methods capable of transmucosal absorption of an active compound through the oral mucosa to the systemic circulatory system. The only reference in Kanios to any dosage form being applied to the oral mucosa is in the background of the art referring to a local anesthesia (Kanios, col. 1, lines 46-55) and at col. 6, lines 59-61, again referring only to a local anesthesia composition. Moreover, in both instances, Kanios fails to disclose any buccal spray composition.

Column 9, lines 7-28 of Kanios read as follows (emphasis added):

> The composition in question can then be applied to a flexible backing or a combination of backings which will serve to define the size and shape of a single dosage of the composition. Such backing may be a three dimensional material such as paper, a non-woven fabric or a natural or synthetic polymer substance. Methods of coating backings are well-known in the art and include techniques involving Mayer rod, gravure, and knife-over roll. Further processing of backings may involve the use of converting equipment for die cutting.
>
> The finished dosage form will be substantially occlusive to water permeation in in vivo.
>
> For example, in one embodiment, the anesthetic agents are dissolved in a solvent, preferably a polyhydric alcohol, and then the resulting mixture is added to an adhesive prior to being placed onto the flexible form or backing. In another embodiment, the resulting mixture is an cream gel, emulsion lotion, salve, plaster, paste, ointment, spray-solution or other "non-finite" composition. The final form which the composition of the invention will be applied depends upon the anatomical site of application and ease of access.

Thus, the finished dosage form of Kanios is made of a composition of an active agent and either a finite or non-finite pharmaceutical carrier (i.e., the "resulting mixture" in col. 9, lines 21 and 23). There is no disclosure in Kanios that the "resulting mixture" is a finished dosage form to be administered directly to the oral mucosa. Instead, according to Kanios, the resulting mixture is made into a "finished dosage form" by applying a flexible backing which further defines the size and shape of the finished dosage form, which is, among other things, occlusive to water permeation in vivo. In contrast to the present invention, Kanios never discloses a finished dosage form in the form of a spray, much less a buccal spray capable of providing a systemic effect when administered to the oral mucosa.

Moreover, Applicant's method claims 62, 63, 122 and 123 require "spraying the oral mucosa" of an animal with the claimed buccal spray composition. Kanios does not contain one iota of any disclosure or suggestion of spraying any finished dosage form or Kanios' intermediate pharmaceutical carrier/active mixture on the oral mucosa.

In addition, the Applicant's claims require that the buccal spray composition is capable of providing transmucosal absorption to the systemic circulatory system. Kanios nowhere discloses this property, which is required by each of Applicant's claims, in any of the topical, locally-acting, dosage forms disclosed in Kanios. Kanios does not even remotely disclose or suggest the claimed property in any buccal spray. It is respectfully submitted that the Office Action employs a reconstruction using portions of the Kanios disclosure out of context and improper hindsight reasoning. See, e.g., In re Fine, 837 F.2d 1071, 1075 (Fed. Cir. 1988).

There is absolutely no disclosure or suggestion in Kanios of a composition that is capable of providing transmucosal absorption of the active compound through the oral mucosa of a mammal to the systemic circulatory system, as presently claimed. Kanios merely discloses local anesthetic agent compositions that are applied topically and then have a local effect. While Kanios refers to a shotgun list of pharmaceutical agents, there is, however, no disclosure or suggestion of a buccal spray composition capable of providing transmucosal absorption of an active compound to the systemic circulatory system, as presently claimed.

Moreover, Applicant's method claims expressly recite spraying the oral mucosa and providing the active to the systemic circulatory system. Kanios' topical, locally-acting final dosage forms cannot be used in such method and Kanios simply never discloses or suggests a method of spraying the oral mucosa, much less of administering an active compound to the systemic circulatory system via spraying the oral mucosa.

According to the Office Action, Kanios lacks disclosure of propellants, but "[i]t would have been obvious to a person of ordinary skill ... to have modified the spray formulations of Kanios by adding a suitable propellant as taught by Purewal with the reasonable expectations of preparing a spray formulation containing propellants which assist in delivery of medicaments to the desired site and ultimately potentiates its absorption." Office Action at 4 (emphasis added).

Purewal does not remedy the deficiencies of Kanios, which, as explained above, does not fairly teach or suggest any "spray formulations" as final dosage form. Purewal refers to an aerosol formulation comprising a medicament; a surfactant; 1,1,2,2-tetrafluoroethane and at least one compound having a polarity higher than 1,1,2,2-tetrafluoroethane. Purewal's formulation is "suitable for delivery to the lung by inhalation." (Purewal at col. 10, lines 14-23, emphasis added). To establish *prima facie* obviousness, the prior art reference(s) must teach or suggest all of the claim limitations. In re Royka, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974). Because neither Kanios or Purewal discloses or suggests any buccal spray, the cited references cannot render any of Applicant's composition claims obvious for at least this reason. Like Kanios, Purewal also fails to disclose or suggest a composition that is adapted for transmucosal absorption of the active compound through the oral mucosa when administered to a mammal to provide the active compound in the systemic circulatory system of the mammal. Instead, Purewal discloses that its aerosol formulations are inhaled. Therefore, Purewal is directed to a different route of administration than the claimed methods and compositions and cannot remedy any of the deficiencies of Kanios as explained above.

In addition, contrary to the Office Action's assertions, one of ordinary skill in the art would not have been motivated to combine the teachings of Kanios with those of Purewal. The Office Action alleges that it would have been obvious to combine the propellants disclosed in Purewal with the "spray formulations of Kanios" to prepare a spray formulation with a propellant. Contrary to the Office Action's position, Kanios discloses no such spray formulation dosage forms and it would not have been obvious to combine the propellants of Purewal's inhalation sprays with the intermediate "resulting mixture" of Kanios, or with the flexible, finite or solid dosage forms, of Kanios. One of ordinary skill would have no motivation to add a propellant to either an intermediate non-finite cream, gel, or spray, etc., or to a flexible solid finished dosage form as taught by Kanios. Accordingly, Applicant submits that the combination of art is improper. In any event, no such combination would achieve what the present Applicant has achieved, buccal spray compositions and methods for attaining systemic circulatory effects.

Accordingly, the rejection of claims 26, 30-31, 37-40, 42, 46-49 and 54-56 based on Kanios in view of Purwal should be withdrawn.

Claims 33-60 and 93-96 stand rejected under 35 U.S.C. § 103(a) as being obvious over Kanios and Purewal et al., as above, and further in view of U.S. Patent No. 5,364,616 to Singer et al. ("Singer"). Applicant respectfully traverses.

Singer refers to methods for preventing or treating gingivitis (inflammation of the gums) or periodontitis (inflammation of the tissue that support the teeth) comprising topically administering to gingival tissue of the oral cavity a composition comprising a safe and effective amount of a selective histamine-2 receptor antagonist compound (See, e.g., Singer, col. 2, lines 32-37 and col. 1, lines 16-17 and 26-27).

The Office Action cites Singer for allegedly disclosing concentration ranges and examples of flavoring agents. The mere disclosure of concentration ranges and examples of flavoring agents does not overcome the deficiencies in Kanios and Purewal, i.e., that unlike the Applicant's claimed invention, the prior art discloses no buccal sprays, much less buccal sprays capable of systemic active ingredient effect.

To treat gingivitis or peridontitis one would want the composition to remain in the oral cavity and not to be delivered to the systemic circulatory system. Indeed, Singer states that the disclosed "topical, oral carrier" denotes a composition "which is administered topically to the oral cavity, held therein for a period of time, and then is largely expectorated rather than being swallowed" (See, e.g., Singer, column 15, lines 26-30). There is no disclosure or suggestion in Singer of a buccal spray capable of transmucosal absorption to provide an active compound to the systemic circulatory system, as presently claimed.

The proper inquiry for obviousness is whether the references disclose each and every feature of the claim (See, e.g., MPEP, 1242) and whether the references suggest the invention and provide one of ordinary skill in the art with a reasonable expectation of

success. In re Vaeck, 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991); In re O'Farrell 853 F.2d 894, 7 U.S.P.Q. 2d 1673 (Fed. Cir. 1988). Neither Kanios, Purewal, nor Singer render the present claims obvious since none of the references, either alone or in combination, (a) discloses each and every feature of the invention and (b) provides a reasonable expectation of success. There is no disclosure or suggestion in either Kanios, Purewal, or Singer of a buccal spray composition capable of being applied to the oral mucosa to provide an active compound to the systemic circulatory system or any disclosure or how to get a systemic effect via a buccal spray composition or method. Furthermore, neither Kanios, Purewal, or Singer, either individually or in combination, provide the required reasonable expectation that a composition applied to the oral mucosa could provide an active compound to the systemic circulatory system, as presently claimed.

For the above reasons, Applicant respectfully requests that the rejections under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

Double Patenting

Claims 32-38, 41, 54, 60-63, 92-100, 103, 116 and 122-123 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting over the claims of co-pending Application Nos. 10/327,195 and 10/726,625. As this rejection is provisional, Applicant will respond with a Terminal Disclaimer or otherwise upon the indication of allowable subject matter.

Conclusion

In view of the above, Applicant believes the pending application is in condition for allowance. If the Examiner should believe that anything further may be required to place this application in even better form for allowance, she is cordially invited to telephone the Applicant's undersigned representative.

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Respectfully submitted,

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